Answer 1:

Bibliographic Information

Potent therapeutic activity of irinotecan (CPT-11) and its schedule dependency in medulloblastoma xenografts in nude mice.
Vassal, Gilles; Boland, Isabelle; Santos, Alexandre; Bissery, Marie-Christine; Terrier-Lacombe, Marie-Jose; Morizet, Jackie; Sainte-Rose, Christian; Lellouch-Tubiana, Arielle; Kalifa, Chantal; Gouyetre, Alain. Laboratory of Pharmacotoxicology and Pharmacogenetics (CNRS URA147), Institut Gustave-Roussy, Villejuif, Fr. International Journal of Cancer (1997), 73(1), 156-163. Publisher: Wiley-Liss, CODEN: IJCNAW ISSN: 0020-7136. Journal written in English. CAN 128:18460 AN 1997:693561 CAPLUS

Abstract

The anti-tumor activity of irinotecan (CPT-11), a DNA-topoisomerase I inhibitor, was evaluated in 5 advanced stage s.c. medulloblastoma xenografts in nude mice, using different schedules of administration. With a 5-day schedule, the highest i.v. dose tested (40 mg kg-1 day-1) induced complete regressions in all xenografts but 1, and delays in tumor growth always exceeded 30 days. Two xenografts, IGRM11 and IGRM33, were highly sensitive, and animals survived tumor-free beyond 120 days after treatment. CPT-11 clearly retained its anti-tumor activity at a lower dosage (27 mg kg-1 day-1). CPT-11 was significantly more active than cyclophosphamide, thiotepa and etoposide against the 3 xenografts evaluated. To study the schedule dependency of its anti-tumor activity, CPT-11 was given i.v. at the same total doses over the same period (33 days) using either a protracted or a sequential schedule in IGRM34-bearing mice. With a dose of 10 mg kg-1 day-1 given on days 0-4, days 7-11, days 21-25 and days 28-32 (total dose, 200 mg kg-1), 3 of 6 animals were tumor free on day 378. The same total dose given with a sequential schedule, i.e., 20 mg kg-1 day-1 on days 0-4 and days 28-32, failed to induce complete regression. The plasma pharmacokinetics of CPT-11 and SN-38 (active metabolite of CPT-11) were studied in IGRM34-bearing animals after a single i.v. dose of 10 and 40 mg kg-1. The plasma clearance rate of CPT-11 was dose dependent. The ratio between the SN-38 and CPT-11 area under the curve in plasma was 0.4-0.65, i.e., significantly higher than that obsd. in humans at the max. tolerated dose (0.01-0.05). Conversely, this ratio was 10-fold lower in tumor than in plasma. Clin. development of irinotecan is warranted in pediatric malignancies.

Answer 2:

Bibliographic Information

Studies on chemotherapy for adenocarcinoma of the uterine cervix using xenografts transplanted in nude mice.
Yamagishi, Masaji. Fac. Med., Toyama Med. Pharm. Univ., Toyama, Japan. Nippon Sanka Fujinka Gakkai Zasshi (1991), 43(2), 165-72. CODEN: NISFAY ISSN: 0300-9165. Journal written in Japanese. CAN 115:341 AN 1991:400341 CAPLUS

Abstract

Adenocarcinoma of the human uterine cervix was successively transplanted into nude mice and the effects of chemotherapy on adenocarcinoma of uterine cervix were investigated in this transplanted tumor. First, it was confirmed that both the original tumor and the transplanted tumor were apparently histol. the same as adenocarcinoma of the uterine cervix (endocervical type). And the transplanted tumor was shown to have the features of adenocarcinoma by an electron microscope. The doubleing time of the transplanted tumor was 9.2 days. For the chemotherapy study, first the therapeutic effects of 11 kinds of agents were screened by single-agent chemotherapy applied to the transplanted tumor. From the results of this series, 6 regimens for multi-agent chemotherapy were tried on the transplanted tumor. The effects of the chemotherapy were evaluated following Battelle Columbus Labs. Protocol and histopathol. The relative regression rates for the tumors treated with mitomycin C (MMC) + cyclophosphamide (CPM) and MMC + CPM + methotrexate (MTX) were 72.99 and 80.9% (Tn/To = 0.84), resp. The results suggest that the combinations of MMC + CPM or MMC + CPM + MTX are regimens that are possibly effective on the adenocarcinoma of human uterine cervix and are worth be trying clin.

Answer 3:

Bibliographic Information

Experimental chemotherapy of human medulloblastoma cell lines and transplantable xenografts with bifunctional alkylating agents. Friedman, Henry S.; Colvin, O. Michael; Skapek, Stephen X.; Ludeman, Susan M.; Elion, Gertrude B.; Schold, S. Clifford, Jr.; Jacobsen, Phillip F.; Muhlbaier, Lawrence H.; Bigner, Darell D. Med. Cent., Duke Univ., Durham, NC, USA. Cancer Research (1988), 48(15), 4189-95. CODEN: CNREA8 ISSN: 0008-5472. Journal written in English. CAN 109:142110 AN 1988:542110 CAPLUS

Abstract

A series of bifunctional alkylators were tested against the genotypically and phenotypically heterogeneous continuous human medulloblastoma cell lines TE-671, Daoy, and D283 Med in vitro and against TE-671 and Daoy growing as s.c. and intracranial xenografts in athymic mice. Drugs tested included melphalan, cyclophosphamide, iphosphamide, phenylketocyclophosphamide, thiotepa, 1,3-bis(2-chloroethyl)-1-nitrosourea (in vivo), and busulfan (in vivo). Melphalan and phenylketocyclophosphamide were the most active agents in vitro, with drug concns. at which there is a 90% redn. in the no. of colonies of 2.13, 5.29, and 4.72 μM for melphalan and 4.60, 5.01, and 4.34 μM for phenylketocyclophosphamide against TE-671, D283 Med, and Daoy, resp. Melphalan, cyclophosphamide, iphosphamide, phenylketocyclophosphamide, and thiotepa produced significant growth delays against s.c. TE-671 and Daoy xenografts, while no activity could be demonstrated for 1,3-bis(2-chloroethyl)-1-nitrosourea or busulfan. Melphalan, cyclophosphamide, iphosphamide, and thiotepa also produced significant increases in median survival in mice bearing intracranial TE-671 and Daoy xenografts. These results extend previous studies demonstrating the antitumor activity of N- and phosphoramide mustard-based bifunctional alkylating agents in the treatment of human medulloblastoma continuous cell lines and transplantable xenografts, and support the continued use of these agents in clin. trials.

Answer 4:

Bibliographic Information

Use of heterotransplants in diffusion chambers for determining the individual drug sensitivity of human ovarian cancer to chemotherapeutic drugs. Sobol, I. L.; Marenich, A. F. Cancer Res. Cent., Moscow, USSR. Byulleten Eksperimental'noi Biologii i Meditsiny (1979), 88(8), 243-5. CODEN: BEBMAE ISSN: 0365-9615. Journal written in Russian. CAN 91:150972 AN 1979:550972 CAPLUS

Abstract

The sensitivity of 10 ovarian tumor heterotransplants in diffusion chambers in mice to hexamethylmelamine [645-05-6], cyclophosphane [50-18-0], 5-fluorouracil [51-21-8], methotrexate [59-05-2], dactinomycin [50-76-0], 17-hydroxyprogesterone caproate [630-56-8], and thiotepa [52-24-4] was variable. E.g., hexamethylmelamine, cyclophosphane, 5-fluorouracil, and methotrexate had a brief inhibiting effect in growth of a solid glandular cancer, inhibited growth of a glandular papillary cancer, and had no effect on growth of a papillary adenocarcinoma. In 4 of 5 cases where results of these expts. were compared with results of expts. obtained in the treatment of patients with the same drugs, exptl. results correlated with clin. findings.